

Online supplementary file 2

Mycoplasma genitalium incidence, persistence, concordance between partners and progression: systematic review and meta-analysis

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Supplementary text, Text S1 to Text S4

Text S1. Medline search strategy

- 1: „Mycoplasma genitalium”[Mesh]
- 2: Mycoplasma genitalium
- 3: 1 OR 2

- 4: "Mycoplasma Infections"[Mesh]
- 5: Mycoplasma
- 6: Mycoplasm*
- 7: 4 OR 5 OR 6

- 8: "Reproductive Tract Infections"[Mesh]
- 9: genital tract
- 10: reproductive tract

- 11: "Salpingitis"[Mesh]
- 12: Salpingitis
- 13: "Endometritis"[Mesh]
- 14: Endometritis
- 15: "Parametritis"[Mesh]
- 16: Parametritis
- 17: "Oophoritis"[Mesh]
- 18: Oophoritis
- 19: Ovary
- 20: Metritis
- 21: Pelviperitonitis

- 22: "Pelvic Inflammatory Disease"[Mesh]
- 23: p.i.d.
- 24: pelvis
- 25: pelvic
- 26: Adnexitis

- 27: "Sexually Transmitted Diseases"[Mesh]
- 28: sexually transmitted
- 29: STD
- 30: STDs
- 31: VD
- 32: Sexual disease transmission
- 33: Venereal
- 34: Venereal

- 35: Genital*
- 36: Vagina*
- 37: Endometri*
- 38: Cervix
- 39: Cervical*
- 40: Urethra*
- 41: Fallopian
- 42: tuba*
- 43: tube
- 44: tubes
- 45: 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44
- 46: 3 OR (7 AND 45)

Filters: 1981/01/01 – 2018/17/03
Humans

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Text S2. Embase search strategy

- 1: 'mycoplasma genitalium'/exp
- 2: Mycoplasma genitalium
- 3: 'mycoplasma genitalium'
- 4: 1 OR 2 OR 3

- 5: 'mycoplasmosis'/exp
- 6: 'mycoplasma'/exp
- 7: 'mycoplasma'
- 8: mycoplasm*
- 9: 5 OR 6 OR 7 OR 8

- 10: 'genital tract infection'/exp
- 11: genital tract
- 12: reproductive tract

- 13: 'adnexitis'/exp
- 14: adnexitis
- 15: ',metritis'/exp
- 16: Metritis
- 17: 'endometritis'/exp
- 18: Endometritis
- 19: Parametritis
- 20: ',ovary inflammation'/exp
- 21: Ovary
- 22: 'pelvipерitonitis'/exp
- 23: pelvipерitonitis
- 24: 'pelvis abscess'/exp
- 25: pelvis abscess
- 26: 'salpingitis'/exp
- 27: salpingitis

- 28: 'pelvic inflammatory disease'/exp
- 29: p.i.d.
- 30: pelvic
- 31: pelvis

- 32: sexually transmitted
- 33: sexual disease transmission
- 34: std
- 35: stds
- 36: vd
- 37: venereal
- 38: venereal

- 39: Genital*
- 40: Vagina*
- 41: Endometri*
- 42: Cervi*
- 43: Urethra*
- 44: Fallopian
- 45: tuba*
- 46: tube
- 47: tubes
- 48: 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47

- 49: 4 OR (9 AND 48)

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Text S3. Additional databases (IndMED, LILACS, African Index Medicus)

„*Mycoplasma genitalium*“

Abbreviations: IndMED, Indian Medical Journals; LILACS Latin American and Caribbean Health Sciences Literature

Text S4. Assessment of risk of bias and reporting

We based our assessment on two tools. We first applied a tool based on a tool for evaluating prevalence studies [1] because we had used this tool in a systematic review of prevalence studies of chlamydia infection [2] and in our linked systematic review of prevalence of *M. genitalium* [3]. We used this tool for cross-sectional studies of concordance. The tool includes elements of both risk of bias and reporting. We used the items about reporting of confidence intervals and raw data for all study designs [1]. We used the classification of responses ('yes', 'no', 'unclear/not reported') in both assessment tools.

For cohort studies and nested case-control studies, which were the study designs used for incidence and persistent detection of *M. genitalium* and risk of progression from lower genital tract *M. genitalium* to PID, we used relevant items from the Cochrane Collaboration Methods Group Tool to Assess Risk of Bias in Cohort Studies [4]. For consistency across study designs, we used the items about the source population from the tool for evaluating prevalence studies to assess selection of exposed and non-exposed cohorts (item 1). We did not assess matching on prognostic variables (item 4) but we used item 5 (assessment of presence or absence of prognostic factors). We only assessed co-interventions (item 8) for studies of PID.

References

1. Boyle MH. Guidelines for evaluating prevalence studies. *Evidence-Based Mental Health* 1998;1(2):37-40.
2. Redmond SM, Alexander-Kisslig K, Woodhall SC, et al. Genital chlamydia prevalence in Europe and non-European high income countries: systematic review and meta-analysis. *PLoS One* 2015;10(1):e0115753.
3. Baumann L, Cina M, Egli-Gany D, et al. Prevalence of *Mycoplasma genitalium* in different population groups: systematic review and meta-analysis. *Sex Transm Infect* 2018;94(4):255-62.
4. Cochrane Collaboration. Tool to Assess Risk of Bias in Cohort Studies. <<https://methods.cochrane.org/bias/sites/methods.cochrane.org.bias/files/public/uploads/Tool%20to%20Assess%20Risk%20of%20Bias%20in%20Cohort%20Studies.pdf>>, (accessed 20 December 2018.).

Supplementary figures and tables, Figure S1 and Figure S2, Table S1 to Table S11

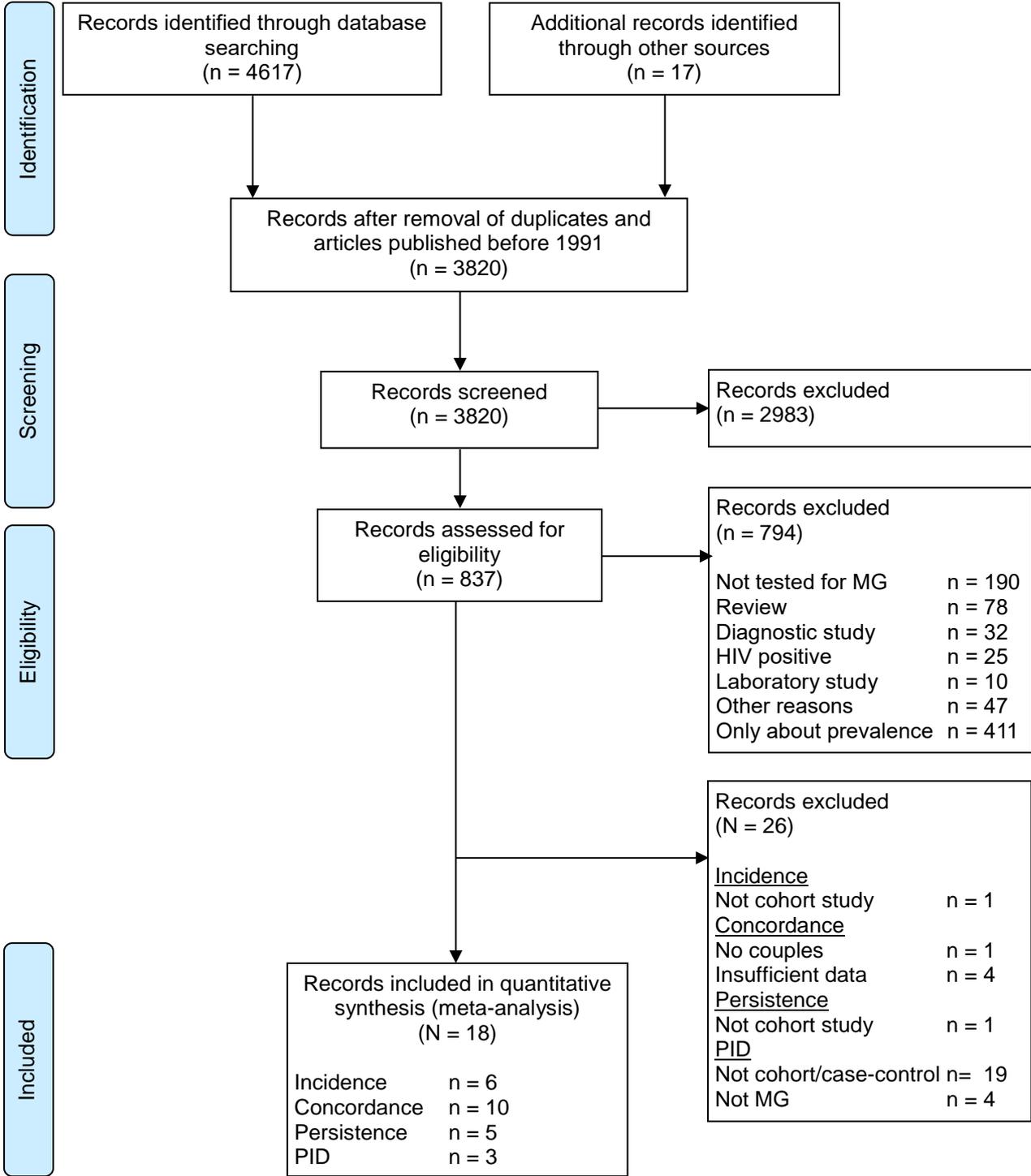


Figure S1. Flow Chart

Abbreviations: MG, *Mycoplasma genitalium*; HIV, human immunodeficiency virus; PID, pelvic inflammatory disease

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Table S1. List of included studies with study name, references, and linked references from systematic review of *M. genitalium* prevalence

Study identifier	References	Linked reference from review of <i>M. genitalium</i> prevalence ^a
Australia 3 [29]	Walker J, Fairley CK, Bradshaw CS, et al. Mycoplasma genitalium incidence, organism load, and treatment failure in a cohort of young Australian women. Clin Infect Dis 2013;56(8):1094-100.	Walker J, Fairley CK, Bradshaw CS, et al. The difference in determinants of Chlamydia trachomatis and Mycoplasma genitalium in a sample of young Australian women. BMC Infect Dis 2011;11:35.
Australia 6 [40]	Slifirski JB, Vodstrcil LA, Fairley CK, et al. Mycoplasma genitalium Infection in adults reporting sexual contact with infected partners, Australia, 2008-2016. Emerging Infectious Diseases 2017;23(11):1826-33.	
Great Britain 2 [5]	Oakeshott P, Aghaizu A, Hay P, et al. Is Mycoplasma genitalium in women the "New Chlamydia?" A community-based prospective cohort study. Clin Infect Dis 2010;51(10):1160-6.	Same
Great Britain 8 [34]	Keane FE, Thomas BJ, Gilroy CB, et al. The association of Mycoplasma hominis, Ureaplasma urealyticum and Mycoplasma genitalium with bacterial vaginosis: observations on heterosexual women and their male partners. Int J STD AIDS 2000;11(6):356-60.	
Great Britain 9 [33]	Keane FE, Thomas BJ, Gilroy CB, et al. The association of Chlamydia trachomatis and Mycoplasma genitalium with non-gonococcal urethritis: observations on heterosexual men and their female partners. Int J STD AIDS 2000;11(7):435-9.	
Kenya 2 [26]	Cohen CR, Nosek M, Meier A, et al. Mycoplasma genitalium infection and persistence in a cohort of female sex workers in Nairobi, Kenya. Sex Transm Dis 2007;34(5):274-9.	
Kenya 3 [28]	Lokken EM, Balkus JE, Kiarie J, et al. Association of recent bacterial vaginosis with acquisition of Mycoplasma genitalium. Am J Epidemiol 2017;186(2):194-201.	

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Study identifier	References	Linked reference from review of <i>M. genitalium</i> prevalence ^a
Peru 1 [35]	Nelson A, Press N, Bautista CT, et al. Prevalence of sexually transmitted infections and high-risk sexual behaviors in heterosexual couples attending sexually transmitted disease clinics in Peru. <i>Sex Transm Dis</i> 2007;34(6):344-61.	
Sweden 2 [36]	Falk L, Fredlund H, Jensen JS. Symptomatic urethritis is more prevalent in men infected with <i>Mycoplasma genitalium</i> than with <i>Chlamydia trachomatis</i> . <i>Sex Transm Infect</i> 2004;80(4):289-93.	Same
Sweden 5 [37]	Anagrius C, Lore B, Jensen JS. <i>Mycoplasma genitalium</i> : prevalence, clinical significance, and transmission. <i>Sex Transm Infect</i> 2005;81(6):458-62.	Same
Sweden 10 [41]	Bjartling C, Osser S, Persson K. The association between <i>Mycoplasma genitalium</i> and pelvic inflammatory disease after termination of pregnancy. <i>BJOG</i> 2010;117(3):361-4.	
Sweden 11 [38]	Falk L, Fredlund H, Jensen JS. Signs and symptoms of urethritis and cervicitis among women with or without <i>Mycoplasma genitalium</i> or <i>Chlamydia trachomatis</i> infection. <i>Sex Transm Infect</i> 2005;81(1):73-8.	
Sweden 12 [39]	Wikstrom A, Jensen JS. <i>Mycoplasma genitalium</i> : a common cause of persistent urethritis among men treated with doxycycline. <i>Sex Transm Infect</i> 2006;82(4):276-9.	
USA/Kenya 1 [30]	Balkus JE, Manhart LE, Lee J, et al. Periodic presumptive treatment for vaginal infections may reduce the incidence of sexually transmitted bacterial infections. <i>J Infect Dis</i> 2016; 213: 1932-7	
Uganda 1 [27]	Vandepitte J, Weiss HA, Kyakuwa N, et al. Natural history of <i>Mycoplasma genitalium</i> infection in a cohort of female sex workers in Kampala, Uganda. <i>Sex Transm Dis</i> 2013;40(5):422-7.	Vandepitte J, Muller E, Bukonya J, et al. Prevalence and correlates of <i>Mycoplasma genitalium</i> infection among female sex workers in Kampala, Uganda. <i>J Infect Dis</i> 2012;205(2):289-96.

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Study identifier	References	Linked reference from review of <i>M. genitalium</i> prevalence ^a
USA 6 [42]	Haggerty CL, Totten PA, Astete SG, et al. Failure of cefoxitin and doxycycline to eradicate endometrial <i>Mycoplasma genitalium</i> and the consequence for clinical cure of pelvic inflammatory disease. <i>Sex Transm Infect</i> 2008;84(5):338-42.	
USA 7 [31]	Tosh AK, Van Der Pol B, Fortenberry JD, et al. <i>Mycoplasma genitalium</i> among adolescent women and their partners. <i>J Adolesc Health</i> 2007;40(5):412-7.	
USA 8 [32]	Thurman AR, Musatovova O, Perdue S, et al. <i>Mycoplasma genitalium</i> symptoms, concordance and treatment in high-risk sexual dyads. <i>Int J STD AIDS</i> 2010;21(3):177-83.	

^a Baumann L, Cina M, Egli-Gany D, et al. Prevalence of *Mycoplasma genitalium* in different population groups: systematic review and meta-analysis. *Sex Transm Infect* 2018;94:255-62.

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Table S2. Included studies, incidence of *M. genitalium*, by study name

Study identifier	First author	Year	Type of specimen collected for analysis	Infectious state of participants at start of study	Number of participants at baseline	Frequency of follow-up	Duration of follow-up	Reported outcome
Australia 3 [29]	Walker J	2013	Vaginal swab	Uninfected and infected participants without treatment	1110	Every six months	12 months	1.3 incident infections per 100 person-years (95% CI, .8, 2.3)
Great Britain 2 [5]	Oakeshott P	2010	Vaginal swab	Uninfected participants	2300	One follow up	Median 16 months	0.91% incident infections per year (95% CI, 0.46%, 1.63%)
Kenya 2 [26]	Cohen CR	2007	Cervical swab and endometrial biopsy	Uninfected and infected participants without treatment	299	Every two months	Up to 33 months	22.7 incident infections per 100 women-years
Kenya 3 [28]	Lokken EM	2017	Vaginal swab	Uninfected and infected participants without treatment	280	Every month	Not reported	34.6 incident infections per 100 person-years (95% CI, 26, 42)
Uganda 1 [27]	Vandepitte J	2013	Cervical swab	Uninfected participants	111	Every three months	12 months	6.6 recurrent infections per 100 person-years (95% CI, 4.8, 9.0)
USA/Kenya 1 [30]	Balkus JE	2016	Genital swab	Uninfected participants	101	Every two months	12 months	40.3 incident infections per 100 person-years (95% CI, 28.5, 56.9)

Abbreviations: CI, confidence interval

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Table S3. Risk of bias assessment, studies reporting incidence of *M. genitalium*, by study name

Study	Target population clearly defined? (yes, no)	Source population clearly defined? (yes, no)	Source population adequate sample of target population? (yes, no)	Can we be confident in the assessment of the exposure? (yes, no)	Can we be confident in the assessment of incident infections? (yes, no)	Can we be confident in the assessment of the presence or absence of prognostic factors? (yes, no)	Can we be confident that individuals lost to follow-up are similar to individuals followed-up until end of study? (yes, no, unclear/not reported)	Proportion of participants lost to follow-up adequate? ($< 20\%$, $20-30\%$, $> 30\%$, unclear/not reported)	Confidence intervals included for incidence? (yes, no)	Data provided to calculate reported result? (yes, no)	Data provided to calculate 95% CI for reported result? (yes, no)
Australia 3 [29]	Red	Green	Red	Green	Green	Red		Orange	Green	Green	Green
Great Britain 2 [5]	Green	Green	Green	Green	Green	Red	Red	Red	Green	Red	Red
Kenya 2 [26]	Green	Green	Green	Red	Green	Green			Red	Green	Green
Kenya 3 [28]	Red	Green	Red	Red	Green	Red			Green	Green	Green
Uganda 1 [27]	Green	Green	Green	Red	Green	Red			Green	Green	Green
USA/Kenya 1 [30]	Red	Green	Red	Red	Green	Red			Green	Green	Green

Adapted from: Cochrane Collaboration. Tool to Assess Risk of Bias in Cohort Studies.

<http://methods.cochrane.org/bias/sites/methods.cochrane.org/files/public/uploads/Tool%20to%20Assess%20Risk%20of%20Bias%20in%20Cohort%20Studies.pdf> >, (accessed 21 December 2018.)

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Table S4. Included studies, duration of persistent detection of *M. genitalium*, by study name

Study identifier	First Author	Year	Type of specimen collected for analysis	Number of participants at baseline	Duration of follow-up	Reported information about persistence	Efforts made to differ persistent infections from reinfections	Antibiotic treatment for other STI
Great Britain 2 [5]	Oakeshott P	2010	Vaginal swab	78	Median 16 months	7 of 27 women had persistent positive samples after 12-27 months	Genotyping	Treatment (not further specified) for <i>C. trachomatis</i> at baseline in intervention arm of the clinical trial. Possible testing and treatment before follow-up.
Kenya 2 [26]	Cohen CR	2007	Cervical swab and endometrial biopsy	107	Up to 33 months	56 (52%), 18 (17%), 10 (9%), and 23 (21%) <i>M. genitalium</i> infections persisted for 1, 3, 5, and 7 months	Genotyping in 7 selected women persistently infected for 10 months or more	Visits every two months. Doxycycline or ciprofloxacin if infected with <i>C. trachomatis</i> or <i>N. gonorrhoeae</i> within four days after diagnosis
Kenya 3 [28]	Lokken EM	2017	Vaginal swab	280	170.5 person years at risk	18, 7 and 3 <i>M. genitalium</i> infections persisted after 100, 200 and 300 days	Not reported	Monthly visits. Immediate syndromic treatment or treatment after diagnosis for sexually transmitted infections according to Kenyan national guidelines.
Uganda 1 [27]	Vandepitte J	2013	Cervical swab	148	12 months	Only graphical presentation	Not reported	Visits every three months. Treatment for vaginal discharge syndrome with doxycycline, ciprofloxacin, metronidazole. Immediate syndromic treatment or as soon as laboratory results available.
USA 7 [31]	Tosh AK	2007	Women: Vaginal specimen	23	12 weeks after positive sample	31.3% of the infections lasted >8weeks 21.9% of the infections lasted >12weeks	Short test intervals (weekly)	Treatment for <i>N. gonorrhoeae</i> , <i>C. trachomatis</i> , <i>T. vaginalis</i> , candidiasis or bacterial vaginosis according to CDC guidelines within two weeks of diagnosis after every three months.

Abbreviations: CDC, Centers for Disease Control and Prevention; STI, sexually transmitted infection; PID, pelvic inflammatory disease

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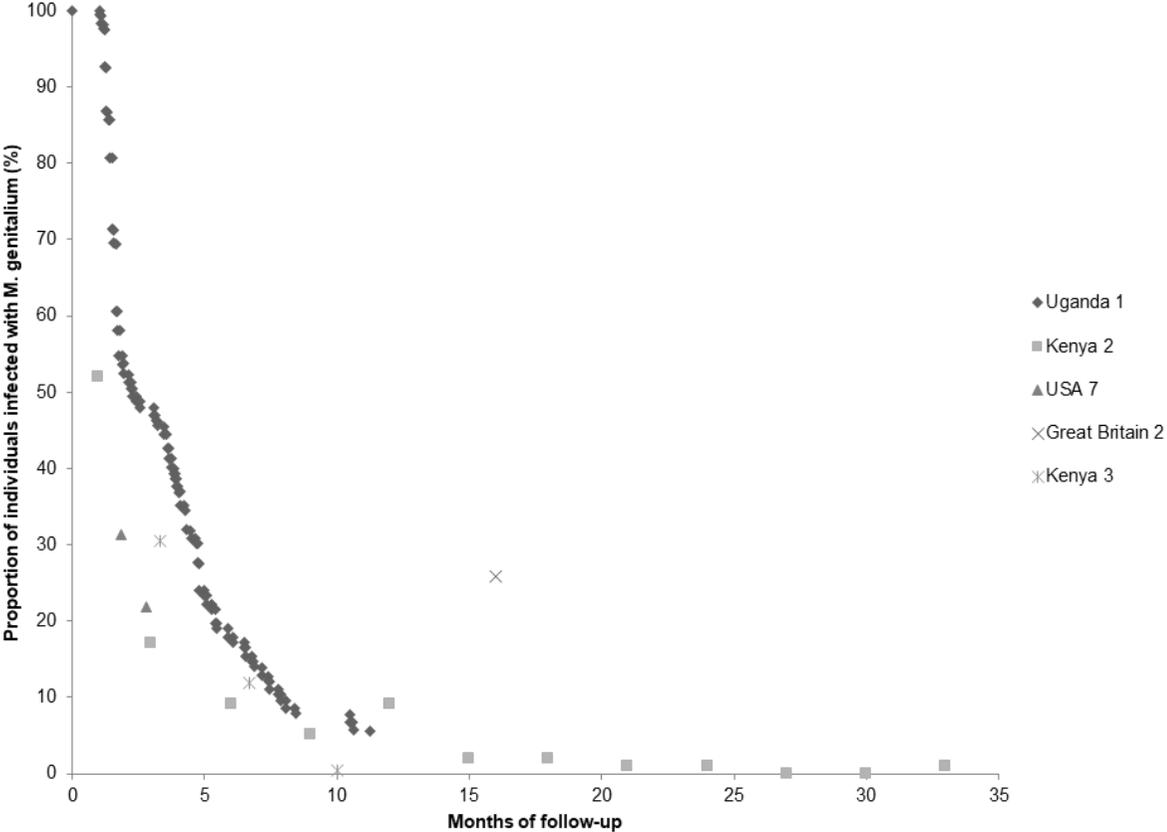


Figure S2. Persistent detection of *M. genitalium*, shown as proportion of infected individuals over time. Each study started with 100% infected individuals at baseline.

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Table S5. Risk of bias assessment, studies reporting duration of persistent detection of *M. genitalium*, by study name

Study	Target population clearly defined? (yes, no)	Source population clearly defined? (yes, no)	Source population adequate sample of target population? (yes, no)	Can we be confident in the assessment of exposure? (yes, no)	Can we be confident in the assessment of the presence or absence of prognostic factors? (yes, no)	Can we be confident in the assessment of outcome? (yes, no)	Can we be confident that individuals lost to follow-up are similar to individuals followed-up until end of study? (yes, no, unclear/not reported)	Proportion of participants lost to follow-up adequate? (< 20%, 20-30%, > 30%, unclear/not reported)	Confidence intervals for reported result included? (yes, no)	Data provided to calculate reported result? (yes, no)
Great Britain 2 [5]	Green	Green	Green	Green	Red	Green	White	Red	Green	Green
Kenya 2 [26]	Green	Green	Green	Red	Green	Red	White	White	Red	Green
Kenya 3 [28]	Red	Green	Red	Red	Red	Red	White	White	Red	Green
Uganda 1 [27]	Green	Green	Green	Red	Green	Red	White	White	Red	Green
USA 7 [31]	Green	Green	Green	Red	Red	Red	White	White	Red	Red

Adapted from: Cochrane Collaboration. Tool to Assess Risk of Bias in Cohort Studies.

<<http://methods.cochrane.org/bias/sites/methods.cochrane.org/files/public/uploads/Tool%20to%20Assess%20Risk%20of%20Bias%20in%20Cohort%20Studies.pdf>> (accessed 21 December 2018).

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Table S6. Included studies, concordance of *M. genitalium* status between sexual partners, by study type and study name

Study identifier	First author	Year	Study design	Type of specimen collected for analysis	Enrolment procedure	Number of couples/number of index cases
Great Britain 8 [34]	Keane FEA	2000	Partner study	Women: Vaginal and endocervical sample Men: Urine sample	Participants approached in STI clinics and asked to invite their current sexual partner if he/she was not yet present	34
Great Britain 9 [33]	Keane FEA	2000	Partner study	Women: Vaginal and endocervical sample Men: Urine sample	Participants approached in STI clinics and asked to invite their current sexual partner if he/she was not yet present	29
Peru 1 [35]	Nelson A	2007	Partner study	Women: Clean-catch urine, pharyngeal, rectal, vaginal, endocervical swab Men: Clean-catch urine, pharyngeal, rectal, urethral swab	Participants approached in STI clinics and asked to invite their current sexual partner if he/she was not yet present	195
USA 7 [31]	Tosh AK	2007	Partner study	Women: Vaginal specimen Men: Urine sample	Recent sexual partners of participants approached by telephone calls or field visits	117
USA 8 [32]	Thurman AR	2010	Partner study	Women: Urine and endocervical sample Men: Urine sample	STI clinic attendees with a positive test for a non <i>M. genitalium</i> STI were asked to bring their current sexual partner to a research clinic	494
Australia 6 [40]	Slifirski JB	2017	Index cases	Women: mostly vaginal or endocervical samples; anorectal sample if anal sex Men: mostly first void urine; anorectal sample if anal sex	People attending as contacts of a person with <i>M. genitalium</i> and lab result of the positive index case	377
Sweden 2 [36]	Falk L	2004	Index cases	First void urine	Current sexual partners of <i>M. genitalium</i> positive index cases asked to come to the clinic by their partner or by partner notification	18
Sweden 5 [37]	Anagrius C	2005	Index cases	Women: Endocervical sample, placed in tube with first void urine Men: First void urine	Current sexual partners of <i>M. genitalium</i> positive index cases asked to come to the clinic by their partner or by partner notification	52

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Sweden 11 [38]	Falk L	2005	Index cases	Women: First void urine and endocervical sample Men: First void urine	Current sexual partners of <i>M. genitalium</i> positive index cases asked to come to the clinic by their partner or by partner notification	21
Sweden 12 [39]	Wikstrom A	2006	Index cases	First void urine	Current sexual partners of <i>M. genitalium</i> positive index cases asked to come to the clinic by their partner or by partner notification	9

Abbreviations: STI, sexually transmitted infection

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Table S7. Risk of bias assessment, concordance of *M. genitalium* status, by study type and study name

Study	Target population clearly defined? (yes, no)	Source population clearly defined? (yes, no)	Source population adequate sample of target population? (yes, no)	Response rate at baseline (>80%, 70-80%, > 70%, unclear/not reported)	Similar socio-demographic attributes of responders and non-responders? (yes, no, unclear/not reported)	Was a probability sampling used? (yes, no, unclear/not reported)	Was a sample size calculation reported? (yes, no, unclear/not reported)	Was the achieved sample size at least as good as in the sample size calculation? (yes, no, unclear/not reported)	Can we be confident in the assessment of exposure? (yes, no)	All data about infectious state of couples provided? (yes, no)
Great Britain 8 [34]	Red	Green	Red	Red		Red			Green	Green
Great Britain 9 [33]	Red	Green	Red			Red			Green	Red
Peru 1 [35]	Green	Green	Red	Red		Red			Green	Red
USA 7 [31]	Green	Green	Green			Red			Green	Red
USA 8 [32]	Green	Red	Red			Red			Green	Green
Australia 6 [40]	Green	Green	Green			Red			Red	Red
Sweden 2 [36]	Green	Green	Green			Red			Green	Green
Sweden 5 [37]	Green	Green	Green			Red			Red	Green
Sweden 11 [38]	Green	Green	Green			Red			Green	Green
Sweden 12 [39]	Green	Green	Green			Red			Green	Green

Adapted from: Redmond SM, Alexander-Kisslig K, Woodhall SC, et al. Genital chlamydia prevalence in Europe and non-European high income countries: systematic review and meta-analysis. *PLoS One* 2015; **10**(1): e0115753.

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Table S8. Test of interaction for study design concordance studies

Sex of index cases	Average difference in mean between index case studies and partner studies	Standard error	95% CI difference	t	P>t	Residual I², %
Male	0.117	0.083	-0.313 to 0.313	1.42	0.198	21.7
Female	0.023	0.145	-0.332 to 0.377	0.16	0.881	67.0

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Table S9. Included studies, progression to PID, by study type and study name

Study identifier	First author	Year	Study type	Sampling method	Type of specimen collected for analysis	Diagnosis of PID	Number of participants at baseline	Duration of follow-up	Result
Great Britain 2 [5]	Oakeshott P	2010	Cohort study	Convenience sample	Vaginal swab	CDC Guidelines 2010. Hager's criteria. Women were also categorized as having PID if a health care professional had treated them for PID.	2378	12 months	PID in <i>M. genitalium</i> positives: 3.9% PID in <i>M. genitalium</i> negatives: 1.7% Absolute risk increase: 2.2%
USA 6 [42]	Haggerty CL	2008	Cohort study	Convenience sample	Cervical swab & endometrial biopsy	At least five neutrophils in the endometrial surface epithelium in the absence of menstrual endometrium and/or at least two plasma cells in the endometrial stroma in the endometrial biopsy.	682	30 days	PID in <i>M. genitalium</i> positives: 6.8% PID in <i>M. genitalium</i> negatives: 7% Absolute risk increase: 0.2%
Sweden 10 [41]	Bjartling C	2010	Nested case-control study	Convenience sample	Urine & cervical or vaginal swab	CDC Guidelines 2010	2079	6 weeks	<i>M. genitalium</i> positive with PID: 12.2% <i>M. genitalium</i> negative with PID: 2.4%

Abbreviations: PID, pelvic inflammatory disease; CDC, Centers for Disease Control and Prevention

CDC Guidelines 2010 for the diagnosis of PID/Modified Hager's criteria: No cause for the illness other than PID identified and one or more of cervical motion tenderness, uterine tenderness and adnexal tenderness present on pelvic examination. Diagnosis made more specific by one or more of: oral temperature >101° F (>38.3° C), abnormal cervical or vaginal mucopurulent discharge, presence of abundant numbers of WBC on saline microscopy of vaginal fluid, elevated erythrocyte sedimentation rate, elevated C-reactive protein and laboratory documentation of cervical infection with *N. gonorrhoeae* or *C. trachomatis*.

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Table S10. Risk of bias assessment, prospective studies reporting progression to PID, by study type and study name

Study	Can we be confident in the assessment of the presence or absence of prognostic factors? (yes, no)	Can we be confident in the assessment of outcome? (yes, no)	Can we be confident that individuals lost to follow-up are similar to individuals followed-up until end of study? (yes, no, unclear/not reported)	Proportion of participants lost to follow-up adequate? (< 20%, 20-30%, > 30%, unclear/not reported)	Can we be confident that co-interventions were similar between groups? (e.g. antibiotic treatment?) (yes, no)	Confidence intervals included for the association of PID with M. genitalium? (yes, no)	Data provided to calculate the odds/risk ratio for the association of PID with M. genitalium? (yes, no)
Great Britain 2 [5]							
USA 6 [40]							
Sweden 10 [41]							

Abbreviations: PID, pelvic inflammatory disease

Cochrane Collaboration. Tool to Assess Risk of Bias in Cohort Studies.

<<http://methods.cochrane.org/bias/sites/methods.cochrane.org.bias/files/public/uploads/Tool%20to%20Assess%20Risk%20of%20Bias%20in%20Cohort%20Studies.pdf>>, (accessed 21 December 2018).

Online supplementary file 2

Table S11. Infection parameters for *M. genitalium* and *C. trachomatis* in studies with data about both infections

Study ID	Study population	Infection	Prevalence, % (95% CI)	Incidence, per 100 person-years (95% CI)	Persistence of untreated infection, from study, median years	Persistence as prevalence/incidence, years	References
Australia 3 [29]	Young women aged 16-25 years; primary health clinics in Australia	MG	2.4 (1.5, 3.3)	1.3 (0.7, 2.2)	Not measured	1.85	MG, CT prevalence: Walker J, Fairley CK, Bradshaw CS, et al. BMC Infect Dis 2011;11:35.
		CT	4.9 (2.9, 7.0)	4.4 (3.3, 5.9)	Not measured	1.11	MG incidence: Walker J, Fairley CK, Bradshaw CS, et al. Clin Infect Dis 2013;56(8):1094-100.
Great Britain 2 [5]	Female students aged ≤27 years; London universities and further education colleges, Great Britain	MG	3.3 (2.6, 4.1)	0.9 (0.5, 1.6)	1.33	3.66	MG prevalence, incidence, persistence, CT prevalence: Oakeshott P, Aghaizu A, Hay P, et al. Clin Infect Dis 2010;51(10):1160-6.
		CT	5.8	Not measured	Not measured	Could not calculate	
Kenya 2 [26]	Female sex workers aged 18-35 years; Kariobangi Nairobi City Council, Nairobi, Kenya	MG	16	22.7 (17.9, 28.3)	0.083	0.7	MG prevalence, incidence, persistence, CT prevalence, incidence: Cohen CR, Nosek M, Meier A, et al. Sex Transm Dis 2007;34(5):274-9.
		CT	8	14.1	Not measured	0.57	

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Kenya 3 [28]	Female sex workers, median age 35.3 years; municipal STI clinic Mombasa, Kenya	MG	16.1	34.6 (26.3, 44.6)	0.23	0.47	MG prevalence, incidence, persistence: Lokken EM, Balkus JE, Kiarie J, et al. Am J Epidemiol 2017;186(2):194-201. CT prevalence, incidence: Masese L. Baeten JM, Richardson BA, et al. Sex Transm Dis 2013;40(3):221-5.
		CT	1.9	5.0	Not measured	0.38	
Uganda 1 [27]	Female sex workers aged 18-40 years; red light areas within southern Kampala, Uganda	MG	14.0 (12.0, 17.0)	6.6 (4.7, 9.0)	0.18	2.12	MG, CT prevalence: Vandepitte J, Muller E, Bukonya J, et al. J Infect Dis 2012;205(2):289-96. MG incidence, persistence: Vandepitte J, Weiss HA, Kyakuwa N, et al. Sex Transm Dis 2013;40(5):422-7.
		CT	9 (7, 11)	Not measured	Not measured	Could not calculate	
USA/Kenya 1 [30]	High-risk women aged 18-45 years; research clinics in Mombasa and Nairobi, Kenya and Birmingham, USA	MG	8	40.3 (28.5, 56.9)	Not measured	0.2	Balkus JE, Manhart LE, Lee J et al. J Infect Dis 2016 ; 213 : 1932-7
		CT	7	15.6 (9.3, 26.4)	Not measured	0.4	
USA 7 [31]	Women aged 14-17 years and their partners; urban primary health care centres, Indianapolis, USA	MG	0.8	Not reported	≥12 weeks in 21.9% 3 month data collection periods	Could not calculate	MG prevalence, persistence: Tosh AK, Van Der Pol B, Fortenberry JD, et al. J Adolesc Health 2007;40(5):412-7. CT prevalence, incidence Batteiger BE, Tu W, Ofner S, et al. J Infect Dis 2010;201(1):42-51.
		CT	10.2	34	Not measured	0.3	

Abbreviations: CT, *C. trachomatis*; MG, *M. genitalium*